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BIOGRAPHY

In Memoriam

Shibasáburo, Baron Kitasato

1852-1931

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Shibasáburo, Baron Kitasato.

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(Plate XLV.)

By the death of Baron Kitasato on 13th June 1931 Japan has lost its most famous bacteriologist and the world a man who made for himself an enduring name in the history of medicine. He was particularly known for three bacteriological discoveries of first-rate importance. In 1889 he cultivated for the first time the bacillus of tetanus in a pure state and having done so he was able to determine with remarkable accuracy the pathology of the disease. In 1890 Kitasato conjointly with Emil Behring made the great discovery of antitoxic sera and in 1894 Kitasato by himself discovered the plague bacillus and worked out in a convincing manner and in record time the ætiology and pathology of plague. It is given to few workers in a generation to establish a finer record.

Shibasáburo Kitasato was born in Ogiungo a mountain village in the prefecture of Kumamoto in the island of Kiushiu. The year of his birth has been given variously as 1854, 1856 and even 1858. The translation of Japanese chronology into English is not easy and not always certain. I have taken trouble to determine Kitasato's age and I am informed by a high Japanese authority after consulting Japanese works of reference that he was born in the "fifth year of Kae" which works out at December 1852. If this is correct Kitasato was in his seventy-ninth year at the time of his death.

In the obituary notice written by his pupil Professor Miyajima (*Brit. Med. Journ.*, 1931, i. 1141) we are told that Kitasato began the study of medicine in the recently established medical school of Kumamoto and, later, he migrated to Tokio to the Government medical college which afterwards became the Tokio Imperial University and there he took his M.D. degree in 1883. He then entered the service of the Central Bureau of Public Health of the Department of the Interior.

In 1885 he was sent by the Japanese Government to study bacteriology in Berlin under Robert Koch who was then nearing the height of his fame. Kitasato remained with Koch at the Hygienisches Institut from 1885 to 1891 first as pupil and later as an independent worker with the title of Honorary Professor in the University of Berlin.

Robert Koch was a dominating personality, and on all his pupils that I have ever met he had the power to arouse extraordinary enthusiasm and admiration for his scientific achievements and also affection for his personal qualities. Kitasato was no exception to the rule and on him Koch's effect was magical and lasting. To the end of his life he strove to justify his association with Koch and ever spoke of it with the highest pride. Long years after their happy and successful Berlin days Koch visited Japan (1908) and his old pupil, now a famous man, received him with open arms and was in the forefront of the Japanese medical profession in making Koch's visit to Nippon almost a national event. Kitasato was also instrumental in raising a monumental stone to Koch at Kamakura (on the Sagami bay of the Kamagawa peninsula near Yokohama.) This *Gedenkstein* has an inscription in Japanese so full of veneration and affection and so simple and beautiful that I am tempted to quote its words. It runs: "*In the forty-second year of the reign of Meiji in the seventh month the great German professor and teacher Koch, professor in Berlin, came to Kamakura. He pitched his tent here on the mountain of spirits and morning and evening he walked about with Professor Kitasato to enjoy the beauty of the mountain and the temple. He returned to his western home where he died not long afterwards. The owner of the mountain has joined with others in erecting this monument in commemoration of Koch's loved spot. This place was chosen as one around which the waves of the sea dash and storm and above which gleams the snow-white peak of Fuji-no-yama already renowned in olden times through the great battle of the famous Japanese hero, General Nitta. Here by Inamurasaki he cast his sword into the sea and hither came the great man across the ocean, looked across to Fuji and loved the place. Therefore let this stone remain here as a lasting memorial.*"

"*Written in the first year of the reign of Taisho in the ninth month, by Nagasaka Shuki.*"

There is something impressive in the veneration of Kitasato for Koch for Miyajima tells us that he erected a shrine to Koch in the inner court of his institute and on the anniversary day of Koch's death (27th May 1910) he commemorated with appropriate Shinto rites the memory of the soul which had departed.

But, let us return to the youthful days of Kitasato in Berlin when he went to Koch's Institute in 1885. Bacteriology had established itself as a progressive science through the discoveries of Pasteur in France and of the Ex-Kreisphysikus Robert Koch in Germany. In

S. Kitasato

particular the simple methods of pure cultivation on solid transparent media which Koch had devised in 1881 had already yielded an amazing harvest of results which had created a revolution in the ideas held on the causation of disease. In addition to a large number of saprophytes the ætiological agents of many important diseases were disclosed with bewildering rapidity by Koch's methods and by himself and his pupils. The new era in medicine was ushered in by Koch's own discovery of the tubercle bacillus in 1882. In the same year Loeffler and Schütz discovered the cause of glanders. In 1884 Koch discovered the vibrio choleræ, Loeffler the diphtheria bacillus and Gaffky the typhoid bacillus.

It was to Berlin—to Koch's Institute—where all this extraordinary activity was in full swing that Kitasato came in 1885. During his stay in Berlin other ætiological agents of disease were added to the list. Much detailed work required, however, to be done. After mastering the exact technique of Koch at the fountain head, Kitasato ardently pursued his researches as an independent worker and soon began to be known outside Berlin. He published papers on the resistance of cholera vibrios to heat and their viability in fæces. In 1889 he grew the remarkable musk-smelling *Fusisporium moschatum,* and in the same year published his classical researches on the ætiology and pathology of tetanus. Nicolaier, 1884, had shown the tetanogenous character of garden earth and J. Rosenbach, 1888, had seen in tetanic discharges the drum-stick bacillus: he tried to grow it, but was not successful. Kitasato succeeded in doing this and showed that it was on obligatory anærobe. He described the effect of the pure cultures of tetanus bacilli on animals. In the body after death from tetanus he was unable to find the tetanus bacillus and inferred that the disease is essentially an intoxication and not due to a dissemination of the bacillus. The actual tetanus toxin was obtained by Faber in 1890. Kitasato also was the first to obtain pure cultures of *B. chauvæi* and in association with Th. Weyl he published valuable papers on anærobic bacteria and the process of anærobiosis in general. He also studied indole production by bacteria.

World-wide fame came to Kitasato at the end of 1890 for on 4th December of that year was published in the *Deutsche medicinische Wochenschrift* his remarkable paper with Emil Behring entitled "Ueber das Zustandekommen der Diphtherie-Immunität und der Tetanus-Immunität bei Thieren." This short communication created a sensation in the medical world for the authors announced that they had been able to produce artificially in animals an immunity against tetanus, and that this immunity depended upon the ability of the cell-free body fluids to render inert the poisons produced by the tetanus bacillus. Behring and Kitasato pointed out that this toxin-destroying—they called it "antitoxic"—property of the blood is still present in the serum after the blood has clotted and that it is so durable that when such serum is injected into the bodies of other animals it can prevent the effect of

multiple lethal doses of tetanus toxin subsequently administered. This antitoxic property is not present in normal serum, not even in that of fowls which are naturally immune to lockjaw. A week after this joint paper by Behring and Kitasato on tetanus, Behring alone published similar results for diphtheria. These two papers laid the basis of serum therapy and originated a new era in therapeutics.

Returning to Japan with a wide bacteriological experience Kitasato established in 1892 a private Institute on a modest scale but it was the first of its kind in Japan and he had the great merit of introducing the study of bacteriology into his native land and by fostering it through many years lived long enough to see a fine flourishing school of scientific workers equal to the best in Europe. In his early struggles Kitasato was greatly aided by Yukichi Fukusawa, a man of high ideals and modern outlook who did much to bring about the extraordinary development of science in Japan during the last twenty years of the nineteenth century. In Tokio, Fukusawa founded the private university of Keiō-Gijiko.

Within a short time of its inauguration Kitasato's Institute was subsidised by the Japanese Government and a new institute was erected at Shiba, a suburb of Tokio. While these things were going on plague had broken out in China and first attracted notice especially in Canton in 1894. The disease was conveyed to Hong-Kong in May of that year and caused great mortality and no little alarm. Theories were rife as to its cause. The Japanese Government sent Kitasato and the pathologist Aoyama to study and report upon the disease. The Japanese mission left Japan on the 5th of June 1894 and landed at Hong-Kong on 12th June and a laboratory was installed in a room in the Kennedy Town Hospital, one of the plague establishments. Work was begun on the 14th of June 1894 and in an autopsy made on that day Kitasato found numerous bacilli in the bubonic lesion as well as in the heart blood, lungs, liver and spleen. As the examination had been made eleven hours after death he was at first doubtful of the significance of the bacilli but he made cultures and inoculated a mouse directly from the spleen and then passed over to the examination of a living case of severe plague. In the peripheral blood he found polar-stained rods and he made cultures which by the following day had shown definite growth at incubation temperature. With these cultures he inoculated mice, guinea-pigs, rabbits and pigeons. All except the pigeon died of a disease similar to plague in man. Every day he examined fresh living cases of plague and from these and from fifteen plague autopsies he found the same bacillus—*Bacillus pestis.* He gave a very accurate account of the microbe and its effects and formulated the general principles for the prevention of plague. Kitasato's work on plague was done quickly and efficiently for within a few days after his arrival in Hong-Kong he had cleared up the mystery of its cause.

Attempts have not been wanting to deprive Kitasato of the full

credit for his discovery and this by some of his own countrymen. Claims have also been put forward on behalf of Alexandre Yersin, a surgeon of the French Colonial Service and director of the Pasteur Institute at Nha Trang (Annam). He also went to Hong-Kong and found a bacillus as the cause of plague. More than thirty years after the events took place the relative merits of Kitasato and Yersin in connection with the discovery of *Bacillus pestis* have again given rise to discussion. I have indicated above the results published by Kitasato and the dates on which he made his observations. Lagrange (*Journ. Trop. Med. and Hygiene*, 1926, xxix. 299) a former assistant of Yersin has written an interesting account of the story. From this it appears that Yersin, who was sent by his Government to Hong-Kong, arrived there on the 15th of June 1894 (the day after Kitasato had begun his work) with very scanty equipment. He saw Kitasato but was unable to converse with him intelligently on account of language difficulties. For some days Yersin could not get any plague autopsies as they were reserved for the Japanese Plague Mission. Yersin examined blood but could find no bacteria in it. His "laboratory" was an open porch and afterwards a straw hut which he was allowed to construct near the Alice Memorial Hospital. On the 20th of June—so Langrange tells us —Yersin got some plague material by tipping English sailors to remove some buboes from the dead bodies in their coffins and in this material he found short bacilli which he was able to cultivate and inoculate into mice and guinea-pigs. On the 23rd of June 1894 he was allowed to make an autopsy or two and he collected some of the bubo juices in tubes and mailed it to France. On the 30th of July, Duclaux read, before the Academie des Sciences, "Extracts from the letters of Yersin" whose own communication was published in the September number of the *Annales de l'Inst. Pasteur* (viii. 662). Kitasato's discovery had already been published in Hong-Kong and a translation had also appeared in the *Lancet* (1894, ii. 428) on August 25th. Such briefly are the facts concerning the discovery of the plague bacillus.

Kitasato continued to take a lively interest in plague and wrote a good deal on the subject in Japanese. In 1911 he went to Manchuria to study the deadly epidemic of pneumonic plague and at the International Plague Conference at Mukden he was elected president. He visited the United States and was at the St Louis Exhibition in 1904. In 1910 he visited England and made himself known to many of the English bacteriologists. In appearance he was short and stout and latterly somewhat corpulent.

In Japan Kitasato spent his life in building up the reputation of his great Institute and developing his school which included pupils with the famous names of Shiga, Hata, and Miyajima. In 1899 Kitasato's Institute was taken over entirely by the Japanese Government and gradually extended till it became a great modern organisation —the Imperial Japanese Institute for Infectious Diseases at Shirokane,

in the Shiba district of Tokio. Kitasato was director of the whole establishment for fifteen years, with great success. For some reason it was then transferred to the control of the Minister of Education and in 1916 was amalgamated with the Imperial University of Tokio. Miyajima (*Brit. Med. Journ.*, 1931, i. 1141) tells us that this change was effected without consulting Professor Kitasato who forthwith resigned his directorship and all his co-workers resigned with him. Whatever was at the back of all this we do not know and it is of no importance for Kitasato's reputation as a scientific worker and one of the founders of modern Japanese scientific medicine which in its output and quality is in the front rank.

In 1914 Kitasato again established a private institute erected in Shirokane Sankocho and named the Kitasato Institute for Infectious Diseases.

In 1916 he was appointed a member of the House of Peers, flung himself into political work and did much to organise the Medical Practitioners' Association in Japan. In recognition of his work in science and in the public services he was raised to the peerage as Baron Kitasato in 1923.

He also founded in 1917 the *Kitasato Archives of Experimental Medicine* and edited this high class scientific journal down to 1930 when his place was taken by Kitashima, Shiga, Hata and Miyajima as editors.

Kitasato received many foreign honours, among them the most treasured being his membership of the Royal Society to which he was elected on the 4th June 1908. He was in fact the only Japanese scientist ever elected to this ancient Society. He was also corresponding member of the Prussian Academie der Wissenschaften, associé étranger of the Académie de Médecine de France, and honorary fellow of the Royal Society of Medicine. There are several portraits of Kitasato in youth and middle age. Our portrait is one of the last taken of him as an elderly man. The cause of his death was apoplexy.

W. BULLOCH.

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